# Therapeutic aspects of herpes genitalis

# A short review

# J. SÖLTZ-SZÖTS AND D. FANTA

From the Epidemiology Unit, Department of Dermatology II, University of Vienna, Vienna, Austria\*

SUMMARY The treatment of manifestations of infection by herpes simplex hominis virus must be aimed at both the local eruptions and the mechanism of recurrence. Recently, some success has been achieved with the use of vaccines and other agents to stimulate a cell-mediated immunity in patients with recurrent herpes infection.

### Local therapy

In recent years the administration of virucidal chemotherapy has increasingly gained ground; in this context it is important that administration starts in the prodromal or initial stage—that is, while the viruses are still multiplying.

#### **ANTIMETABOLITES**

Good results have been obtained with the antimetabolites, 5-iodo-2'desoxyuridine, in ophthalmology. In dermatology, however, because of insufficient penetration of the agent good results can only be obtained in some cases after the addition of dimethylsulphoxide (DMSO).

## TROMANTADINE HYDROCHLORIDE

At present there is no certain knowledge about the interaction between tromantadine hydrochloride, the virus, and the affected cell. Nevertheless, the administration of this compound at an early stage leads either to rapid drying of the herpetic manifestations in a high percentage of cases or to the eruptions subsiding in the prodromal stage (Fanta, 1976). The drawback to its topical administration is that it is a highly sensitising agent which frequently provokes contact dermatitis (Fanta and Mischer, 1976).

\*In co-operation with the Ludwig Boltzmann Institute for Research on Infectious Venereodermatological Diseases.

Address for reprints: Professor J. Söltz-Szöts, Allgemeines Krankenhaus des Stadt Wien, II Universitats-Hautklinik, 9 Alserstrasse 4, A-1090 Vienna, Austria

Received for publication 16 November 1978

#### FLUORESCENT DYES

The administration of heterocyclic fluorescent dyes to acute herpes simplex lesions followed by irradiation (photodynamic inactivation) was recommended for a while (Jarrat and Knox, 1975). There is, however, experimental evidence that photodamaged virus particles—that is, virus particles with DNA changes which no longer produce an infection—have the property of malignant transformation of cultured cells (Duff and Rapp, 1971).

#### Systemic therapy

#### IMMUNE STIMULATION

Attempts at influencing the mechanism of recurrence by immune stimulation are so far based on numerous, partly non-specific, partly specific vaccinations. It should be emphasised that the unpredictable course of the disease makes an evaluation of therapeutic measures difficult.

# Herpes antigen

Considerable improvement can be achieved in 70%-80% of all cases by repeated administrations of herpes antigen. We have used a mixed tissue culture vaccine containing type 1 and type 2 antigens (Söltz-Szöts, 1971a) obtained from cultures of herpes type 1 and 2 in embryonated chicken eggs and subsequently heat-inactivated. The vaccine was standardised by determination of the virus titre with the complement fixation test (Söltz-Szöts, 1971b; Söltz-Szöts and Fanta, 1974).

#### Bacillus subtilis lysage

Bacillus subtilis lysage acts as an active stimulant of the reticuloendothelial system—that is, as a stimulant of immunospecific resistance—and consequently stimulates phagocytosis. Although it is recommended in the treatment of recurrent herpes there are no controlled studies on its efficacy.

#### Levamisole

Levamisole is a widely used anthelmintic agent; it is a chemical derivative of imidazol and has a stimulating effect on reduced cellular immunity (Symoens and Brugmans, 1974). In a double-blind study a significant improvement in recurrent herpes has been obtained (Fanta and Wimmer, 1979).

#### BCG vaccine

In the treatment of tumours as well as of chronic viral and bacterial infections, the stimulation of cell-mediated immunity by vaccination with BCG vaccine has become increasingly importan'. Furthermore, in the treatment of intractable cases of herpes genitalis a positive influence on the course of the disease could be achieved by repeated vaccinations with BCG vaccine. In an unselected group of patients with recurrent herpes a success rate of 60% has been observed; because of the possibility of strong local reactions, however, this treatment is justified only in cases that do not respond to other forms of therapy (Fanta and Wimmer, 1979).

## Interferon

Interferon, with a broad antiviral spectrum, is species-specific, has a better prophylactic than therapeutic effect, and offers short-term protection. Clinical trials with exogenous interferon treatment of herpes virus infections in man have yielded promising results, but these still need to be confirmed on a larger scale by double-blind studies. More extensive clinical use of interferon would firstly require an expansion in production in order to ensure that all patients would receive treatment.

In order to achieve successful treatment with interferon-inducing agents the following criteria should be adopted:

- Administration must start early; once the virus has stopped multiplying no further effect can be obtained.
- (2) The injections must be administered at 24-hourly intervals for a period of about eight days. The interferon-inducing agent must make direct contact with the cell and must, therefore, be administered in high dosages. In our studies of patients with extensive herpes simplex infections treated with an inactivated influenza virus as interferon-inducing agent, the average duration of the disease could be reduced. In addition, the intervals between herpetic recurrences were significantly prolonged when treatment was combined with herpes antigen vaccination (Söltz-Szöts, 1971a, b; 1976).

#### Conclusion

It must be emphasised, however, that despite great progress in the diagnosis, immunology, and treatment of herpes genitalis, we are still only at the beginning, promising as the progress may be.

#### References

Duff, R., and Rapp, F. (1971). Properties of hamster embryo fibroblast transformed *in vitro* after exposure to ultraviolet-irradiated herpes simplex virus type 2. *Journal of Virology*, 8, 469-477.

Fanta, D. (1976). Behandlung des herpes simplex mit tromantadinhydrochlorid. Wiener medizinische Wochenschrift, 126, 315-317.

Fanta, D., and Mischer, P. (1976). Contact dermatitis from tromantadine hydrochloride. Contact Dermatitis, 2, 282-284.

Fanta, D., and Wimmer, F. (1979). Treatment of recurrent herpes with Levamisole. In press.

Jarrat, M., and Knox, J. (1975). Die photodynamische wirkung bei herpes simplex: eine übersicht. Der Hautarzt, 26, 345-348.

Söltz-Szöts, J. (1971a). Die behandlung des rezidivierenden herpes simplex. Zeitschrift für Haut-und Geschlechtskrankheiten, 46, 267-272.

Söltz-Szöts, J. (1971b). Neue methoden bei der behandlung der viruserkrankungen der haut. Zeitschrift für Haut-und Geschlechtskrankheiten, 46, 755-760.

Söltz-Szöts, J., and Fanta, D. (1974). Interferon und interferonstimulierung neue ansätze in der therapie von virusinfektionen. Der Hautarzt, 25, 313-318.

Söltz-Szöts, J. (1976). Therapie der viruserkrankungen der haut. Der Hautarzt, suppl. 1, 111-115.

Symoens, J., and Brugmans, J. (1974). Treatment of recurrent stomatitis and herpes with levamisole. British Medical Journal, 4, 592.